CARDIAC ENLARGEMENT IN U.S. FIREFIGHTERS

Findings and Recommendations from Non-Invasive Identification of Left Ventricular Hypertrophy/ Cardiomegaly in Firefighters

July 19, 2017

National Fallen Firefighters Foundation®

Acknowledgements

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Funding was provided through the Federal Emergency Management Agency (FEMA) Assistance to Firefighters Grant (AFG) program's award EMW-2011-FP-00663 (PI: Dr. S.N. Kales) and EMW-2013-FP-00749 (PI: Dr. D.L. Smith).

Contents

List of Acronyms

BMI	Body Mass Index
CHD	Coronary Heart Disease
CVD	Cardiovascular Disease
LV	Left ventricular
LVH	Left Ventricular Hypertrophy
LVM	Left Ventricular Mass
SCD	Sudden Cardiac Death
ECHO	Echocardiography
CMR	Cardiac Magnetic Resonance
CRF	Cardiorespiratory Fitness
OSA	Obstructive Sleep Apnea

Glossary of Terms

Arrhythmia – irregular heart beat.

Body Surface Area – a measure that reflects that total skin surface area of the human body.

Cardiomegaly – a general term used to describe an enlarged heart; can be caused by various conditions, but often associated with hypertension and coronary artery disease.

Cardiovascular Disease (CVD) – refers to diseases or problems of the heart and/or blood vessels.

Cardiovascular strain – refers to the physiological response of the cardiovascular system to exercise or physical work.

Coronary Heart Disease (CHD) – a narrowing of the blood vessels (coronary arteries) that supply blood and oxygen to the heart tissue; often called coronary artery disease (CAD).

Heart attack – also known as myocardial infarction; occurs when heart's blood supply vessels (coronary arteries) is insufficient preventing the blood supply from reaching the heart.

Left ventricular – largest chamber of the heart responsible for pumping blood out to the brain, other vital organs and the rest of the body.

Left ventricular hypertrophy – a thickening of the heart muscle surrounding the left ventricle, resulting in a greater mass of the heart.

Left ventricular mass index – a measure of left ventricular weight adjusted for body size that derived by dividing LV mass by some a body size parameter (e.g. body surface area, height) to account for physiologic variation related to body size.

Prevalence – a measure to reflect the proportion of a population who has (or had) a specific characteristic in a given time period.

Sudden cardiac death – an unexpected cardiovascular death due to heart attack or arrhythmia, where loss of consciousness occurs abruptly after the onset of symptoms or without warning and death quickly ensues thereafter.

Sudden cardiac event – an unexpected cardiovascular event (stroke, heart attack, heart arrhythmia) that occurs suddenly in a person with or without diagnosed cardiovascular disease. This event may or may not result in death.

Susceptible individuals – those at risk for CVD events because of underlying heart problems (known or unknown).

Purpose and Objectives

This white paper presents attainable and practical approaches to improve firefighter health and safety targeted to fire service leadership and individual firefighters. This is accomplished through the specific objectives identified below.

Objectives

1. To raise awareness within the fire service about enlargement of the heart (including cardiomegaly and left ventricular (LV) hypertrophy) and how it increases the risk of developing CVD and on-duty SCD; as well as it's potential to be treated and reversed if recognized beforehand.
2. To summarize the current challenges we face in the identification of cardiac enlargement in active firefighters according to the method of assessment (see Chapter 1);
3. To more accurately estimate how common cardiac enlargement is among career US Firefighters by combining the use of different imaging modalities along with other comprehensive clinical data (see Chapters 2 and 3);
4. To identify the most important predictors of LV mass in career male firefighters in the United States so that more accurate medical screening programs can be implemented allow for the identification of LV hypertrophy/cardiomegaly in a timely fashion, thus enabling clinical interventions to decrease firefighters' morbidity and mortality (see Chapter 4) .
5. To translate current understanding of research to practical recommendations that the fire service can champion in the areas of medical evaluations, fitness goals, and behavioral health changes. Each of these areas will build on current efforts within the fire service, but will be expanded to include new scientific information, and will be approached with the perspective that we must increase the accessibility of the information by individual firefighters (see Chapter 5).

Executive Summary

This white paper is based on the background, key findings and recommendations of work sponsored by FEMA (US Department of Homeland Security) to better understand cardiac enlargement in the US fire service. Roughly half (45%) of the nation's line-of-duty firefighter fatalities are due to cardiovascular disease (CVD), and about 45% are due to sudden cardiac death (SCD). These events almost always occur in susceptible individuals with underlying heart problems. Unfortunately, many of these heart problems are not recognized during firefighters' careers or go untreated, and this is particularly true of cardiac enlargement. Firefighter autopsy reports demonstrate that a large majority of firefighters succumbing to SCD had significant narrowing of one or more coronary arteries, consistent with coronary heart disease (CHD), which has been the focus of most CVD research in the fire service. Although less well-known, previous research has also shown that a majority of firefighters dying of SCD have had various forms of cardiac enlargement- usually accompanying CHD, but sometimes as the only or predominant heart abnormality.

Cardiomegaly refers to enlargement of the heart in general as well as to an abnormally heavy heart by weight. **Left ventricular (LV) hypertrophy** is a related term that specifically refers to enlargement (measured either as increased wall thickness or elevated weight) of the left ventricle - the chamber of the heart responsible for pumping blood out to the circulation and vital organs. Both LV hypertrophy and cardiomegaly are frequently found during the autopsies of persons who died of SCD. LV hypertrophy/cardiomegaly are structural abnormalities of the heart proven to increase the risk of arrhythmias, myocardial infarction, stroke and the risk of death. Cardiac enlargement is a condition, which renders firefighters susceptible to cardiovascular events up to and including SCD.

Despite the longstanding issue of CVD deaths in the fire service and the frequent observation of LV hypertrophy/cardiomegaly in autopsies, very little is known about these conditions in active firefighters. For example, how common is heart enlargement among working firefighters, what are the best methods of measuring its presence, and which firefighters are at highest risk and therefore, should be screened. It is important to note that if recognized beforehand, effective treatments for LV hypertrophy/ cardiomegaly are available. Thus, it is imperative that we find effective ways to screen firefighters at risk for this condition.

This white paper presents the current challenges that we face in accurately defining cardiac enlargement, provides more definitive estimates of how common it is among active career firefighters, and identifies the most important predictors of cardiac enlargement. Lastly, specific recommendations targeted to different important stakeholders are presented in order to decrease the burdens of CVD and SCD in the fire service.

Firefighters from the Indianapolis Fire Department worked together with research scientists, medical doctors and along with local and national fire service leaders in order to make this project a success. In this report we provide details on a series of studies we conducted so as to describe how common cardiac enlargement is, in a 400 group of occupationally active career firefighters (from the Indianapolis Fire Department) using different imaging techniques and among a group of 353 fallen firefighters from all across the US who suffered on-duty fatalities due to a traumatic, non-cardiac cause, using autopsy data. In both groups of firefighters we investigated the presence of cardiac enlargement and its relationship to to various medical and other factors.

Even though standardization of cardiac enlargement definitions is needed, **our results clearly demonstrate that obesity as measured by body mass index (BMI) drives LV mass, heart weight and LV wall thickness. Therefore, reducing obesity will decrease LV mass, improve CVD risk profiles, and should in turn reduce on-duty CVD events in the fire service, including SCD.**

Our understanding of sudden cardiac events and cardiovascular disease in the fire service has greatly and rapidly increased over the past 15 years due to a shared sense of mission in reducing duty-related cardiac deaths by researchers, fire service representatives, and funding agencies. **But, knowledge alone cannot bring about the needed results. Action is required— recommendations must be actionable, then, adopted and finally, implemented. Adoption of the actionable, evidence-based recommendations in this and previous reports will help the US fire service make significant strides toward reducing duty-related cardiac deaths, with a reduction of at least 30% within reach.**

BMI drives heart weight, left ventricular mass and wall thickness.

Background

Cardiovascular disease (CVD) is the leading cause of on-duty death among US firefighters and an important and costly cause of morbidity. CVD causes about 50% of firefighters' on-duty deaths and, as in the general population, these cardiovascular events are largely due to coronary heart disease (CHD), with Sudden Cardiac Death (SCD) causing 45% of line-of-duty fatalities. [1-4] There is also an increasing recognition in the role of Left Ventricular (LV) hypertrophy/cardiomegaly in the risk of SCD independent of the presence of CHD, although it has long been recognized that individuals dying of CHD tend to have heavier hearts than those dying of non-cardiac causes.[5-7] Moreover, for every fatal on-duty CVD event, there are an estimated 25 nonfatal, line-of-duty CVD events in the US fire service. [8,9] The extent of this problem in the U.S. fire service has not changed significantly in the last two decades, despite major advances in cardiovascular medicine.[1 4,10,11]

Firefighting combines situations that are both physically demanding (intense work, heavy tools & personal protective gear) and psychologically stressful (alarm response, danger) and leads to significant cardiovascular strain.[12,13,14,15] This cardiovascular strain together with environmental hazards (heat stress, noise, dehydration, particulate and gaseous exposures in smoke) can trigger a CVD event in a susceptible or vulnerable individual. [1,16]

Based on a superficial look at the statistics, it may appear that SCD is likely to strike any firefighter, but the risk of sudden cardiac death is not distributed equally or at random within the fire service or over time. On the contrary, research has definitively shown that specific job duties put a firefighter at increased risk of sudden cardiac death, and that the vast majority of SCD events occur among firefighters with underlying heart disease that has made them susceptible. Because firefighting is inherently dangerous and many of its hazards cannot be engineered out of the job, a key prevention question is: what makes individual firefighters most susceptible to CVD events? While a single emergency call may trigger an event, the underlying disease develops as a result of multiple, interacting risk factors gradually over many years (Figure 1). Our group has demonstrated that on-duty CVD events and heart disease retirements occur almost exclusively in firefighters with underlying heart disease, which is associated with an excess of CVD risk factors or a previous diagnosis of CVD.

50%

Percentage of firefighter line-of-duty fatalities attributed to heart attack or stroke.

Enlargement of the heart is considered a structural abnormality of the heart[17,18] and appears to be a key pen-ultimate and predisposing step on the causal pathway that makes a firefighter susceptible to CVD events (Figure 1- orange star). [1,19,20] Cardiomegaly refers to enlargement of the heart in general as well as to an abnormally heavy heart by weight. Most pathologists consider a heart weight above 450 g in a man and 390 g in a woman to be abnormally heavy or consistent with cardiomegaly. Left ventricular (LV) hypertrophy is a related term that specifically refers to enlargement of the left ventricle or the chamber of the heart responsible for pumping blood out to the circulation and vital organs. LV hypertrophy is usually defined as an increased thickness of the left ventricular wall as measured by a pathologist at autopsy or estimated by an imaging technique, or an elevated LV mass or weight of the left ventricle as measured by various imaging techniques. The two most frequently used non-invasive, imaging modalities for the assessment of LV wall and LV mass have been echocardiography (ECHO) and cardiac magnetic resonance (CMR). [21]

Defining the precise cut-off for defining LV hypertrophy is difficult because the value is affected by many parameters, including body size and imaging technique. Furthermore, physical exercise training can increase wall thickness in a way that is generally thought to be healthy or positive. The general consensus is that a wall thickness greater than 1.2 cm is usually an indication of unhealthy LV hypertrophy.

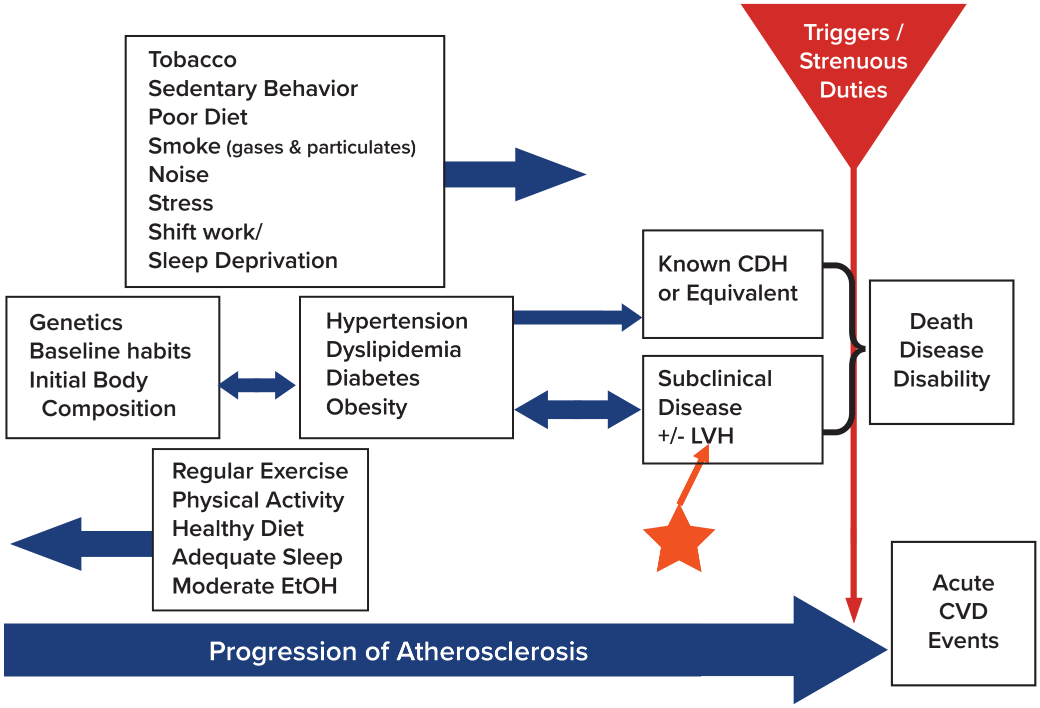
> *Cardiac enlargement is a key predisposing step on the causal pathway that makes a firefighter susceptible to CVD events.*

ECHO and CMR rely on different technologies and use different algorithms for the assessment of LV mass, providing different average values along with different degrees of precision. 22,23,24 The differences between these methods can make the distinctions between disease states and normality harder to make. [25] Evidence suggests an improved prognostic value, when LV hypertrophy is based on the most accurate prediction of LV mass. Both LV mass and heart size increase in proportion to the overall body size and thus differ by gender, with higher values seen in men. [25,26,27] Therefore, body size parameters should be considered to normalize myocardial mass, minimizing the effect of body size in the population distribution.[21] An LV mass “index” is derived by dividing LV mass with height, or by body surface area (BSA), or by comparing it to a reference group of healthy subjects. Height indexing seems to be the most sensitive in identifying obesity-related LV hypertrophy that is associated with CVD events and all-cause death.

LV hypertrophy and cardiomegaly have been widely recognized to increase the risk of lethal ventricular arrhythmias, myocardial infarction and stroke; and are proven to predict CVD and overall mortality in the general population. Unfortunately, these conditions have not been adequately researched in the fire service.[28-32] Current evidence from autopsies on firefighters who succumbed to SCD have shown LV hypertrophy to be common among US firefighters, often co-morbid with CHD and to play a major role in CVD events and SCD risk in the fire service. In fact, the majority of CVD death victims (60-76%) suffered from LV hypertrophy/cardiomegaly, which was usually unrecognized before death.[33,34,35]

Cardiovascular Disease (CVD) Risk Factors

- *Non-modifiable:*
  - *Age*
  - *Sex*
  - *Family history*
- *Modifiable:*
  - *Hypertension*
  - *Overweight/Obesity*
  - *Dyslipidemia*
  - *Diabetes*
  - *Physical inactivity*
  - *Physical Fitness*
  - *Smoking*
  - *Diet*
  - *Sleep quantity/quality*
  - *Stress/Resiliency*



Adapted from: Soteriades et al Kales. *Cardiology in Review.* 2011

Figure 1. Conceptual Model of CVD in the Fire Service: Risk Factors, Progression (left to right) and Triggering of Events (right) in Susceptible Firefighters. Modified from Soteriades at al. (1).

Beyond its role in CVD and the fact that it is likely common, in order to justify screening for LV hypertrophy/cardiomegaly, we also need to recognize that it can be treated and reversed if detected at early stages. The detection of LV hypertrophy by imaging should only very rarely be a career-ending event for a firefighter. In fact, there are several proven effective treatments for LV hypertrophy based on its underlying risk factors, specifically obesity, hypertension and Obstructive Sleep Apnea (OSA).[32,36] Weight loss through both diet and exercise in overweight and obese subjects is particularly beneficial because it can improve OSA, blood pressure control and can reverse obesity-related effects on LV mass.[37] Blood pressure reduction by lifestyle measures and medications in the setting of hypertension, and treatment of OSA with weight loss and continuous positive airway pressure (CPAP) are also effective in reducing/normalizing LV hypertrophy.

Despite the critical prognostic significance of LV hypertrophy/cardiomegaly for CVD and SCD events, its definition demonstrates wide variability among measurement techniques, imaging modalities, normalization processes (adjustments for body size), technicians and institutions.[38,39] Evidence suggests an increasing prognostic value, when LV hypertrophy is based on the accurate assessment of LV mass, with LV mass being an independent predictor for cardiovascular risk.[38,40]

References

1. Soteriades ES, Smith DL, Tsismenakis AJ, Baur DM, Kales SN. Cardiovascular disease in US firefighters: a systematic review. *Cardiology in Review.* Jul-Aug 2011;19(4):202-215.
2. Smith DL, Barr DA, Kales SN. Extreme sacrifice: sudden cardiac death in the US Fire Service. *Extreme physiology & medicine.* 2013;2(1):6.
3. Fahy R, LeBlanc P, Molis J. Firefighter Fatalities in the United States 2011. *National Fire Protection Association, Quincy, MA.* 2012.
4. Fahy R. U.S. Firefighter Fatalities Due to Sudden Cardiac Death, 1995-2004. *National Fire Protection Association, Quincy, MA.* 2005(99):44-47.
5. Kreger BE, Cupples LA, Kannel WB. The electrocardiogram in prediction of sudden death: Framingham Study experience. *American Heart Journal.* Feb 1987;113(2 Pt 1):377-382.
6. Perper JA, Kuller LH, Cooper M. Arteriosclerosis of coronary arteries in sudden, unexpected deaths. *Circulation.* Dec 1975;52(6 Suppl):III27-33.
7. Tavora F, Zhang Y, Zhang M, et al. Cardiomegaly is a common arrhythmogenic substrate in adult sudden cardiac deaths, and is associated with obesity. *Pathology.* Apr 2012;44(3):187-191.
8. Haynes H, Molis J. U.S. Firefighter Injuries-2014. *National Fire Protection Association, Quincy, MA.* 2015.
9. Fahy R, LeBlanc P, Molis J. Firefighter Fatalities in the United States - 2014. *National Fire Protection Association, Quincy, MA.* 2015.
10. Kales SN, Soteriades ES, Christophi CA, Christiani DC. Emergency duties and deaths from heart disease among firefighters in the United States. *The New England Journal of Medicine.* Mar 22 2007;356(12):1207-1215.
11. Fahy R, Molis J. Firefighter Fatalities in the United States-2010. *National Fire Protection Association, Quincy, MA.* 2011.
12. Smith DL, Manning TS, Petruzzello SJ. Effect of strenuous live-fire drills on cardiovascular and psychological responses of recruit firefighters. *Ergonomics.* 2001; 44(3):233-254.
13. Fernhall B, Fahs CA, Horn GP, Rowland T, Smith D. Acute effects of firefighting on cardiac performance. *Euro J of Appl Physiology.* 2012; 112(2):735-741.

14. Fahs CA, Yan H, Ranadire S,Rossow LM, et al. Acute effects of firefighting on arterial stiffness and blood flow. *Vasc Med.* 2011;16(2): 113-118.

15. Smith DL, et al. Clotting and fibrinolytic changes after firefighting activities. *Med Sci Sports Exerc.* 2014; 46(3):448–454.

16. Kales SN, Smith DL. Firefighting and the Heart: Implications for Prevention. *Circulation.* 2017; 135(14):1296-1299.

17. Bluemke DA, Kronmal RA, Lima JA, et al. The relationship of left ventricular mass and geometry to incident cardiovascular events: the MESA (Multi-Ethnic Study of Atherosclerosis) study. *Journal of the American College of Cardiology.* Dec 16 2008;52(25):2148-2155.

18. Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Left ventricular mass and incidence of coronary heart disease in an elderly cohort. The Framingham Heart Study. *Annals of Internal Medicine.* Jan 15 1989;110(2):101-107.

19. Kales SN, Soteriades ES, Christoudias SG, Christiani DC. Firefighters and on-duty deaths from coronary heart disease: a case control study. *Environmental Health: A Global Access Science Source.* Nov 6 2003;2(1):14.

20. Kales SN, Tsismenakis AJ, Zhang C, Soteriades ES. Blood pressure in firefighters, police officers, and other emergency responders. *American Journal of Hypertension.* Jan 2009;22(1):11-20.

21. Armstrong AC, Gjesdal O, Almeida A, et al. Left ventricular mass and hypertrophy by echocardiography and cardiac magnetic resonance: the multi-ethnic study of atherosclerosis. *Echocardiography.* 2014; 31: 12-20.

22. Gidding SS. Controversies in the assessment of left ventricular mass. *Hypertension.* 2010; 56: 26-28.

23. Alfakih K, Bloomer T, Bainbridge S, Bainbridge G, Ridgway J, Williams G, Sivananthan M. A comparison of left ventricular mass between two-dimensional echocardiography, using fundamental and tissue harmonic imaging, and cardiac MRI in patients with hypertension. *Eur J Radiol.* 2004;52:103-109.

24. Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr.* 2005; 18: 1440-1463.

25. Dewey FE, Rosenthal D, Murphy DJ Jr, Froelicher VF, Ashley EA. Does size matter? Clinical applications of scaling cardiac size and function for body size. *Circulation.* 2008; 117: 2279-2287.

26. Kawel-Boehm N, Maceira A, Valsangiacomo-Buechel ER, et al. Normal values for cardiovascular magnetic resonance in adults and children. *Journal of Cardiovascular Magnetic Resonance: Official Journal of the Society for Cardiovascular Magnetic Resonance.* 2015; 17: 29.

27. Brumback LC, Kronmal R, Heckbert SR, et al. Body size adjustments for left ventricular mass by cardiovascular magnetic resonance and their impact on left ventricular hypertrophy classification. I*nt J Cardiovasc Imaging.* 2010; 26: 459-468.

28. James MA, Jones JV. Ventricular arrhythmia in untreated newly presenting hypertensive patients compared with matched normal population. *J Hypertens.* May 1989;7(5):409-415.

29. Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. *The New England Journal of Medicine.* May 31 1990;322(22):1561-1566.

30. Haider AW, Larson MG, Benjamin EJ, Levy D. Increased left ventricular mass and hypertrophy are associated with increased risk for sudden death. *Journal of the American College of Cardiology.* Nov 1998;32(5):1454-1459.

31. Benjamin EJ, Levy D. Why is left ventricular hypertrophy so predictive of morbidity and mortality? *The American Journal of the Medical Sciences.* Mar 1999;317(3):168-175.

32. Bauml MA, Underwood DA. Left ventricular hypertrophy: an overlooked cardiovascular risk factor. *Cleve Clin J Med.* Jun 2010;77(6):381-387.

33. Soteriades ES, Targino MC, Talias MA, et al. Obesity and risk of LVH and ECG abnormalities in US firefighters. *Journal of Occupational and Environmental Medicine / American College of Occupational and Environmental Medicine.* Aug 2011;53(8):867-871.

34. Geibe JR, Holder J, Peeples L, Kinney AM, Burress JW, Kales SN. Predictors of on-duty coronary events in male firefighters in the United States. *The American Journal of Cardiology.* Mar 1 2008;101(5):585-589.

35. Kales SN, Soteriades ES, Christoudias SG, Christiani DC. Firefighters and On-Duty Deaths from Coronary Heart Disease: a Case Control Study. *Environmental Health: A Global Access Science Source.* 2003; 2(1):14.

36. Georgiopoulou VV, Kalogeropoulos AP, Raggi P, Butler J. Prevention, diagnosis, and treatment of hypertensive heart disease. *Cardiology Clinics.* Nov 2010;28(4):675-691.

37. Dela Cruz CS, Matthay RA. Role of obesity in cardiomyopathy and pulmonary hypertension. *Clinics in Chest Medicine.* Sep 2009;30(3):509-523, ix.

38. Armstrong AC, Gidding S, Gjesdal O, Wu C, Bluemke DA, Lima JA. LV mass assessed by echocardiography and CMR, cardiovascular outcomes, and medical practice. *JACC Cardiovasc Imaging.* Aug 2012;5(8):837-848.

39. Armstrong AC, Gjesdal O, Almeida A, et al. Left ventricular mass and hypertrophy by echocardiography and cardiac magnetic resonance: the multi-ethnic study of atherosclerosis. *Echocardiography.* 2014;31(1):12-20.

40. Gidding SS. Controversies in the assessment of left ventricular mass. *Hypertension.* Jul 2010;56(1):26-28.

Chapter 1

Current Challenges in the Identification of Cardiac Enlargement By Imaging Modalities and Autopsies

In light of the amazing advances in imaging techniques available to visualize the heart, it should be easy to measure heart size or weight – but, the truth is, there are multiple challenges to determining accurate size and weight, and even more challenges associated with knowing what size is healthy and what size is pathological (unhealthy) in a given individual.

Evidence suggests an improved prognostic value or better prediction of the risk of future disease, when LV hypertrophy is defined or classified based on accurate estimates of LV mass.[1] Increased LV mass has been shown to be a strong predictor of cardiovascular events among individuals without[2-4] and with prior coronary heart disease[5,6] as well as those with heart failure.[7,8] An increase in LV mass is associated with a higher incidence of cardiovascular events, including death, while a reduction in LV mass is a marker of lower risk for cardiovascular events, especially among individuals on anti-hypertensive treatment.[9,10] Therefore, the correct assessment of LV mass and its change over time are vital to accurately determine prognosis, disease progression and response to therapy.[11] Namely, the accurate evaluation of LV mass is fundamental, not only for the determination of the degree of hypertrophy but also for the assessment of its regression.[9,10,12] Notwithstanding this increasing recognition of the importance of LV mass, the best way to incorporate LV mass measurement into clinical practice has not been firmly established, in the general population or in the fire service, due to a number of controversies.[11,13,14]

LV mass values present a wide distribution among healthy individuals, with distinct differences observed by sex and ethnicity, as well as with the frequency of athletic training. Hence, "anthropometric" parameters (measures of body size), and perhaps, exercise habits should be taken into account to make meaningful comparisons among individuals. Therefore, "indexing" LV mass, using different measures of body size such as height, weight, or body surface area, has been the most common process used in order to compare values among different persons. Accordingly, LV mass indexing has a critical role in defining LV hypertrophy in research studies that attempt to predict cardiovascular risk.[11,13,15-19] And yet, there is currently no universally agreed upon method for normalizing LV mass. This lack of consensus regarding normal values complicates efforts to identify appropriate cut-off values as to when hypertrophy of the left ventricle should be called abnormal and therefore, indicate a need for monitoring and/or treatment.

In addition to inconsistencies in the interpretation of data obtained via different techniques for the normalization of LV mass values, there are also challenges due to different imaging modalities for its assessment. The two most frequently used non-invasive, imaging modalities for the assessment of LV mass have been echocardiography (ECHO) and cardiac magnetic resonance (CMR).[20] ECHO and CMR rely on different technologies and use different algorithms for the assessment of LV mass, providing different average values along with different degrees of precision.[11,21,22] The differences between these methods can make the distinctions between disease states and normality harder to make.[23] In addition, LV mass can also be physiologically increased by healthy behaviors such as endurance physical training, an observation that should be accounted for when establishing LV mass reference values.[24,25,26]

A further complication arises when we attempt to compare heart size at death determined by autopsy with estimates of heart size determined by imaging studies in living persons. During autopsies, total heart weight is routinely assessed, along with LV wall thickness, by dissecting and directly weighing and measuring the heart. However, it is rare for an autopsy to separately weigh the left ventricle and thus, autopsies usually do not quantify LV mass.

Therefore, little is known regarding the relationship of LV mass (determined by imaging) to heart weight (obtained during autopsies), a feature that could facilitate extrapolations or comparisons between imaging modalities and autopsies. Such information would allow us to better utilize data from autopsies in order to make clinical recommendations. The very limited data available at present suggest that LV mass accounts for a greater proportion of total cardiac mass in diseased hearts as compared to normal hearts.

Another area in need of updated information regards the reference ranges for normal heart weights at autopsy. "Normal" values in current use date back to older studies (1970-1990's) conducted when the population was shorter and leaner. Therefore, in light of the global obesity epidemic and the effects of body weight and body size on heart weight, the "normal values" need to be re-addressed.[27-30]

In conclusion, there is ample evidence that increased heart size is associated with negative cardiovasuclar outcomes. Howeveer, there are multiple challenges to determining a specific "cut-off" score that indicates increased risk, and growing recognition that the cut off values may differ based on imaging modality.

References

1. Armstrong AC, Gidding S, Gjesdal O, Wu C, Bluemke DA, Lima JA. LV mass assessed by echocardiography and CMR, cardiovascular outcomes, and medical practice. *JACC Cardiovasc Imaging.* Aug 2012;5(8):837-848.

2. Brumback LC, Kronmal R, Heckbert SR, et al. Body size adjustments for left ventricular mass by cardiovascular magnetic resonance and their impact on left ventricular hypertrophy classification. *Int J Cardiovasc Imaging.* Apr 2010;26(4):459-468.

3. Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. *The New England Journal of Medicine.* May 31 1990;322(22):1561-1566.

4. Tsang TS, Barnes ME, Gersh BJ, Takemoto Y, Rosales AG, Bailey KR, Seward JB (2003) Prediction of risk for first age-related cardiovascular events in an elderly population: the incremental value of echocardiography. *J Am Coll Cardiol.* 2003; (42):1199–1205.

5. Gottdiener JS, Arnold AM, Aurigemma GP, Polak FJ, Tracy RP, Kitzman DW, Gardin JM, Rutledge JE, Boineau RC. Predictors of congestive heart failure in the elderly: the Cardiovascular Health Study. *J Am Coll Cardiol.* 2000; (35):1628–1637.

6. Ghali JK, Liao Y, Simmons B, Castaner A, Cao G, Cooper RS (1992) The prognostic role of left ventricular hypertrophy in patients with or without coronary artery disease. *Ann Intern Med.* 1992; (117):831–836.

7. Pocock SJ, Wang D, Pfeffer MA, Yusuf S, McMurray JJ, Swedberg KB, Ostergren J, Michelson EL, Pieper KS, Granger CB.Predictors of mortality and morbidity in patients with chronic heart failure. *Eur Heart J.* 2006; (27): 65–75.

8. Bluemke DA, Kronmal RA, Lima JA, et al. The relationship of left ventricular mass and geometry to incident cardiovascular events: the MESA (Multi-Ethnic Study of Atherosclerosis) study. *Journal of the American College of Cardiology.* Dec 16 2008;52(25):2148-2155.

9. Dahlof B, Devereux RB, Kjeldsen SE, et al. Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. *Lancet.* Mar 23 2002;359(9311):995-1003.

10. Devereux RB, Wachtell K, Gerdts E, et al. Prognostic significance of left ventricular mass change during treatment of hypertension. *JAMA.* Nov 17 2004;292(19):2350-2356.

11. Gidding SS. Controversies in the assessment of left ventricular mass. *Hypertension.* Jul 2010;56(1):26-28.

12. Okin PM, Devereux RB, Jern S, et al. Regression of electrocardiographic left ventricular hypertrophy by losartan versus atenolol: The Losartan Intervention for Endpoint reduction in Hypertension (LIFE) Study. *Circulation.* Aug 12 2003;108(6):684-690.

13. de Simone G, Devereux RB, Daniels SR, Koren MJ, Meyer RA, Laragh JH. Effect of growth on variability of left ventricular mass: assessment of allometric signals in adults and children and their capacity to predict cardiovascular risk. *Journal of the American College of Cardiology.* Apr 1995;25(5):1056-1062.

14. Foster BJ, Mackie AS, Mitsnefes M, Ali H, Mamber S, Colan SD. A novel method of expressing left ventricular mass relative to body size in children. *Circulation.* May 27 2008;117(21):2769-2775.

15. Mancia G, De Backer G, Dominiczak A, et al. 2007 Guidelines for the management of arterial hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Eur Heart J.* Jun 2007;28(12):1462-1536.

16. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Pediatrics.* Aug 2004;114(2 Suppl 4th Report):555-576.

17. Chirinos JA, Segers P, De Buyzere ML, et al. Left ventricular mass: allometric scaling, normative values, effect of obesity, and prognostic performance. *Hypertension.* Jul 2010;56(1):91-98.

18. Jafary FH, Jafar TH. Disproportionately high risk of left ventricular hypertrophy in Indo-Asian women: a call for more studies. *Echocardiography.* Sep 2008;25(8):812-819.

19. Wong RC, Yip JW, Gupta A, Yang H, Ling LH. Echocardiographic left ventricular mass in a multiethnic Southeast Asian population: proposed new gender and age-specific norms. *Echocardiography.* Sep 2008;25(8):805-811.

20. Armstrong AC, Gjesdal O, Almeida A, et al. Left ventricular mass and hypertrophy by echocardiography and cardiac magnetic resonance: the multi-ethnic study of atherosclerosis. *Echocardiography.* 2014;31(1):12-20.

21. Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr.* Dec 2005;18(12):1440-1463.

22. Hendel RC, Patel MR, Kramer CM, et al. ACCF/ACR/SCCT/SCMR/ASNC/NASCI/SCAI/SIR 2006 appropriateness criteria for cardiac computed tomography and cardiac magnetic resonance imaging: a report of the American College of Cardiology Foundation Quality Strategic Directions Committee Appropriateness Criteria Working Group, American College of Radiology, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, American Society of Nuclear Cardiology, North American Society for Cardiac Imaging, Society for Cardiovascular Angiography and Interventions, and Society of Interventional Radiology. *Journal of the American College of Cardiology.* Oct 3 2006;48(7):1475-1497.

23. Dewey FE, Rosenthal D, Murphy DJ, Jr., Froelicher VF, Ashley EA. Does size matter? Clinical applications of scaling cardiac size and function for body size. *Circulation.* Apr 29 2008;117(17):2279-2287.

24. Gidding SS. Controversies in the assessment of left ventricular mass. *Hypertension.* Jul 2010;56(1):26-28.

25. Estes NA, 3rd, Kovacs RJ, Baggish AL, Myerburg RJ. Eligibility and Disqualification Recommendations for Competitive Athletes with Cardiovascular Abnormalities: Task Force 11: Drugs and Performance-Enhancing Substances: A Scientific Statement from the American Heart Association and American College of Cardiology. *Circulation.* 2015; 132: e330-333.

26. Vanhaebost J, Faouzi M, Mangin P, Michaud K. New reference tables and user-friendly Internet application for predicted heart weights. *International Journal of Legal Medicine.* Jul 2014;128(4):615-620.

27. Mandal R, Loeffler AG, Salamat S, Fritsch MK. Organ weight changes associated with body mass index determined from a medical autopsy population. The American journal of forensic medicine and pathology. Dec 2012;33(4):382-389.

28. James WP. WHO recognition of the global obesity epidemic. I*nternational Journal of Obesity (2005).* Dec 2008;32 Suppl 7:S120-126.

29. Kuczmarski RJ, Flegal KM. Criteria for definition of overweight in transition: background and recommendations for the United States. *The American Journal of Clinical Nutrition.* Nov 2000;72(5):1074-1081.

30. Kitzman DW, Scholz DG, Hagen PT, Ilstrup DM, Edwards WD. Age-related changes in normal human hearts during the first 10 decades of life. Part II (Maturity): A quantitative anatomic study of 765 specimens from subjects 20 to 99 years old. *Mayo Clinic Proceedings.* Feb 1988;63(2):137-146.

Chapter 2

Methods – Study Population 1 (Non-Invasive Assessment/ Imaging)

Male career firefighters, aged 18 years and older were recruited from the Indianapolis Fire Department. Eligible firefighters had no restrictions on duty and had a recorded fire department-sponsored medical exam in the last two years that included a submaximal exercise tolerance test.

From those eligible (n=1059), we selected at random a total of 400 participants, as follows: 100 participants from the entire eligible population; 75 low-risk participants (age <40, non-obese, free of hypertension and high cardiorespiratory fitness) and 225 higher risk participants (at least 2 of the following: age >/=40, obese, HTN or low cardiorespiratory fitness) for further LV hypertrophy / cardiomegaly screening and imaging tests (figure 2). Obesity was defined by standard criteria (BMI >/=30 kg/m2). Hypertension was considered present if resting blood pressure is >/=140/90 mm Hg. Cardiorespiratory fitness (CRF) was determined based on the recorded treadmill time and the estimated maximal aerobic capacity during the last exercise test. Those selected were included in the study if they had no contraindication to CMR and had signed informed consent to participate. Out of the 400 active career firefighters, we excluded 7 participants with missing measurements of LV mass, as assessed by CMR.

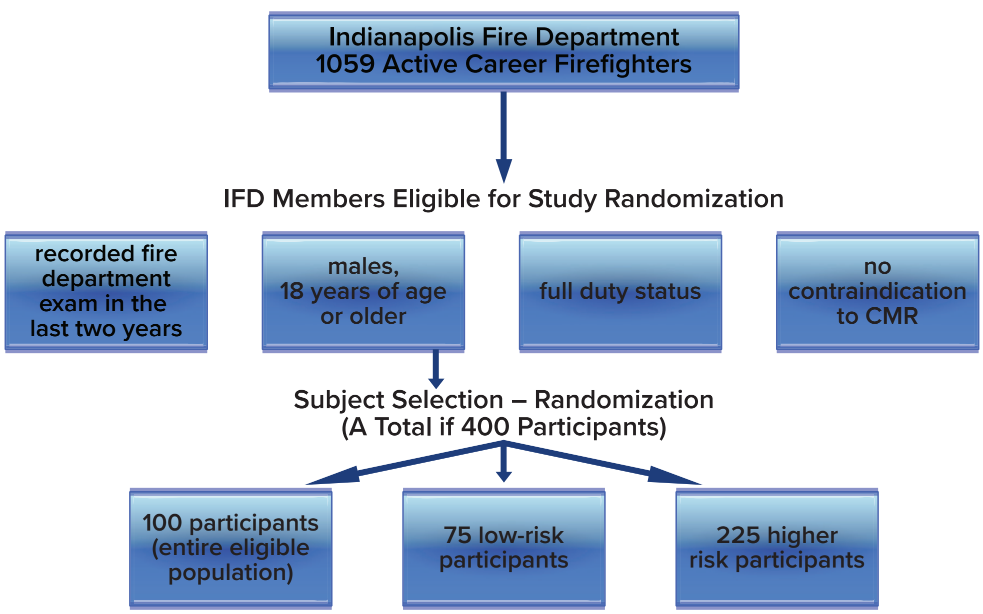


Figure 2. Inclusion Criteria and Subject Selection for further screening with ECHO and CMR

Definitions of Cardiac Enlargement (Non-Invasive Assessment/Imaging)

LV mass was assessed by both ECHO and cardiac MRI (CMR) imaging. First, a transthoracic cardiac echocardiogram was done as a simple two-dimensional (2-D) study with limited m-mode recordings. The echocardiogram is a type of ultrasound test that uses sound waves that are sent through a device called a transducer. The device picks up echoes of the sound waves as they bounce off the different parts of the heart and then these echoes are turned into moving pictures of the heart that can be seen on a video screen. The transthoracic cardiac echo is the most common type, where the views of the heart are obtained by moving the transducer to different locations on the chest or abdominal wall.

An abbreviated CMR was also performed as "function only" immediately after the ECHO. A CMR is a painless imaging test that uses radio waves, magnets, and a computer to create detailed pictures of the heart. CMR can provide detailed information on the type and severity of heart disease to help decide the best way to treat heart problems such as coronary heart disease, heart valve problems, pericarditis, cardiac tumors, or damage from a heart attack. Board certified specialists performed the clinical interpretation of imaging.

LV mass was adjusted in standard fashion for body size by calculating an index. Three sets of commonly used indices were derived, by dividing LV mass in grams with either body surface area that was estimated with the Mosteller formula (in meters2) or body height to the powers of 1.7 and 2.7 (in meters1.7 and meters2.7, respectively).

Assessment of Cardiovascular Risk Factors (Non-Invasive Assessment/ Imaging)

- Height and weight were measured using standard and consistent clinical practices.
- BMI was calculated as the weight in kilograms divided by the square of height in meters.
- Blood pressure was measured using an appropriately sized cuff with the subject in the seated position.
- Heart rate and blood pressure were obtained in a resting state from the physical examination.
- Medical exam data were further supplemented by a questionnaire that was administered before the imaging studies. The survey collected comprehensive information on smoking status, personal history of heart rhythm problems, family history of cardiac problems and moderate to vigorous physical activity level in minutes per week.
- High risk of obstructive sleep apnea (OSA) was assessed using a well-known, validated and commonly used instrument, the Berlin Questionnaire.

Study Population 2: Direct Measures Of Heart Weight And Wall Thickness (Autopsy Reports)

Male non-cardiac traumatic fatalities (deaths due to blunt trauma, burns, or asphyxiation) were identified for 2006 to 2012 from a firefighter autopsy research data bank maintained by the National Fallen Firefighters Foundation. The inclusion criteria for the non-cardiac trauma controls were (1) age ≤ 65 years, (2) duty-related death, and (3) cause of death determined by autopsy to be due to blunt trauma, burns, or asphyxiation and not related to any cardiovascular pathologic entity.

Definitions Of Cardiac Enlargement (Autopsy Reports)

We defined LV hypertrophy quantitatively as a wall thickness greater than 1.2 cm and cardiomegaly as a heart weight greater than 450 grams from autopsy data. We also defined LV hypertrophy and cardiomegaly as qualitatively is discussed in the narrative conclusions of the autopsy report.

Data from 353 autopsy reports were available. We conducted our main analysis with data from 293 autopsy records, excluding those with missing information on BMI. Under the assumption that the pathologists would have reported the weight in the autopsies if this was in the obesity range, we also performed a series of sensitivity analyses with data from all 353 autopsy records, where we estimated how common LV hypertrophy and cardiomegaly were, assuming a BMI of 25 kg/m2 and then 27 kg/m2 for all records with missing information.

Chapter 3

Cardiac Enlargement in U.S. Firefighters: Prevalence Estimates by Echocardiography, Cardiac Magnetic Resonance and Autopsies

The aims of this study were to:

1. estimate the prevalence of cardiac enlargement (including LV hypertrophy) among active US firefighters, and determine how much prevalence estimates vary according to different methods of imaging/assessment and different adjustments for body size. Thus, we derived prevalence estimates for LV hypertrophy among active career firefighters by the two imaging techniques described above (ECHO and CMR).
2. determine prevalence estimates of cardiomegaly and LV hypertrophy from direct measures of heart weight and LV wall thickness at autopsy among the second study population of fallen firefighters who suffered a non-cardiac fatality while on-duty.

Findings

The active career firefighters were screened at an average age of 45.3 years; 45% were obese; 32% had high risk of OSA and 34% had low CRF.

One of the major challenges to assessing LV hypertrophy is that different definitions are available for the definition of LV hypertrophy. There is a wide distribution of LV mass values in a healthy

45%

of firefighters were obese.

32%

of firefighters had high risk of sleep apnea.

34%

of firefighters had low cardiorespiratory fitness.

population and thus anthropometric parameters should be considered to normalize LV mass, minimizing the effect of body size in the population distribution. Therefore, an LVmass "index" is usually derived by dividing LV mass with a body size parameter (i.e. body surface area, height) and then LV hypertrophy is defined by an LVmass "index" greater than some specified cutoff value.[1,2,3] Definitions may vary by the method used (ECHO or CMR) or by the method (unit) of reporting and the body size parameter used to create the index. In fact, using these different definitions we found vary different prevalence estimates of LV hypertrophy by both ECHO and CMR assessment based on different criteria. These findings are summarized in Table 1. For example, indexing LV mass by BSA using CMR measurements was the only criterion to deliver zero prevalence of cardiac enlargement, while all prevalence estimates based on CMR assessments were much lower.

Table 1. LV hypertrophy prevalence estimates by ECHO and CMR.

Imaging Technique	Ranges of prevalence estimates (%)
ECHO	3.3-32.8
CMR	0.0–5.3

In the second group of data, LV hypertrophy and cardiomegaly estimates were based on the numerical values provided in the autopsy reports of the non-cardiac traumatic fatalities are presented in Table 2. Cardiomegaly was defined as a heart weight greater than 450 grams and LV hypertrophy was defined as a LV wall thickness greater than 1.2 cm.

Table 2. LV hypertrophy & cardiomegaly prevalence estimates among non-cardiac traumatic fatalities.

Condition	Prevalence estimates (%)
Cardiomegaly	33.8
LV hypertrophy	41.5

Importantly, further analysis revealed that heart weight and LV wall thickness steadily increased with increasing age and BMI.

Conclusions & Discussion

The present findings in US firefighters demonstrate great variability of the prevalence estimates of LV hypertrophy within and between ECHO and CMR, according to the different criteria utilized. Considerable variance was also observed using direct measures at autopsy, again, depending on the criteria used. Autopsy findings clearly indicated that BMI was a major determinant of heart weight. Prevalence estimates of LV hypertrophy were considerable, for example LV hypertrophy was present at 17.5% of the active career firefighters when using ECHO and indexing to height comparing to 33.8% prevalence based on the autopsies measurements. Although CMR is considered to be the gold standard among imaging techniques, the prevalence estimates of cardiac enlargement currently observed seemed unrealistically low, especially when compared to direct measures at autopsy in a similar firefighter population. Given the great variance in LV mass and LV hypertrophy estimates, surprisingly, average LV wall thickness was similar across both imaging techniques and at autopsies.

Among traumatic deaths, where any possible contribution of cardiac pathology to the death was reasonably excluded, as many as 40% demonstrated cardiomegaly while up to 42% presented LV hypertrophy. This can be explained in large part by the high prevalence of obesity that was documented among those non-cardiac traumatic controls.

In addition our findings suggested the presence of cardiac enlargement to be steadily increasing as a function of BMI. Our findings are consistent with the literature, which finds obesity to be a significant risk factor for LV hypertrophy and increased cardiac mass.[4,5] Furthermore, one could hypothesize that traumatic fatalities occur more frequently in obese firefighters as they could be more inclined to be physically trapped during a fire secondary to their body size and relative physical immobility.[6] In fact, the average BMI of the non-cardiac fatalities was higher than that of the active firefighter study base population (31.2 vs. 30.3) and that previously reported for representative, population-based firefighter samples (28.6 for career firefighters).[7]

To the best of our knowledge, our current study is the first to evaluate the status of cardiac enlargement among active career firefighters by both ECHO and CMR measurements based on different criteria, as well as the first to compare these estimates to those derived from non-cardiac traumatic fatalities. We previously found the prevalence of cardiomegaly to be 22% in a smaller sample of non-cardiac, traumatic firefighter autopsies limited to those under the age of 45 years of age.[6] Our estimates for these age groups were similar, 27% and 24% for those under the age of 35 and 45 years of age respectively. Having access not only to data from active career firefighters, but also to autopsy reports from non-cardiac traumatic fatalities, we relied on quantitative data to estimate the prevalence of cardiac enlargement in the US fire service via several different methods and get a more holistic picture.

Our results highlight the methodological challenges of describing cardiomegaly and LV hypertrophy in any population based on different definitions that are published and used clinically. Given the strong evidence we provide on the association between cardiac enlargement and sudden cardiac death in the fire service, research attention should be focused on this challenge. Irrespective of the variability observed based on the different definitions used, our study clearly revealed BMI as the major driver of heart weight. Thus, attention in the fire service must not await further research, but begin to focus on reducing obesity as a means of decreasing cardiovascular events among firefighters.

References

1. Chirinos, J.A., P. Segers, M.L. De Buyzere, R.A. Kronmal, M.W. Raja, et al. (2010) Left ventricular mass: allometric scaling, normative values, effect of obesity, and prognostic performance. *Hypertension.* 56: 91-8.

2. Armstrong, A.C., O. Gjesdal, A. Almeida, M. Nacif, C. Wu, et al. (2014) Left ventricular mass and hypertrophy by echocardiography and cardiac magnetic resonance: the multi-ethnic study of atherosclerosis. *Echocardiography.* 31: 12-20.

3. Cuspidi, C., S. Meani, F. Negri, V. Giudici, C. Valerio, et al. (2009) Indexation of left ventricular mass to body surface area and height to allometric power of 2.7: is the difference limited to obese hypertensives? *J Hum Hypertens.* 23: 728-34.

4. Soteriades, E.S., D.L. Smith, A.J. Tsismenakis, D.M. Baur, and S.N. Kales (2011) Cardiovascular disease in US firefighters: a systematic review. *Cardiol Rev.* 19: 202-15.

5. Soteriades, E.S., M.C. Targino, M.A. Talias, R. Hauser, I. Kawachi, et al. (2011) Obesity and risk of LVH and ECG abnormalities in US firefighters. *J Occup Environ Med.* 53: 867-71.

6. Yang, J., D. Teehan, A. Farioli, D.M. Baur, D. Smith, et al. (2013) Sudden cardiac death among firefighters </=45 years of age in the United States. *Am J Cardiol.* 112: 1962-7.

7. Poston, W.S., C.K. Haddock, S.A. Jahnke, N. Jitnarin, B.C. Tuley, et al. (2011) The prevalence of overweight, obesity, and substandard fitness in a population-based firefighter cohort. *J Occup Environ Med.* 53: 266-73.

Chapter 4

Effect of Body Mass Index on Left Ventricular Mass in Career Male Firefighters

This chapter presents the key findings from the imaging studies and, thus, identifies the most important predictors of LV mass after indexing for height among career male firefighters as assessed by both ECHO and CMR.

Findings

When assessing the ability of each CVD risk factor to separately predict the LV mass index values, resting systolic blood pressure, hypertension, high risk of OSA, low cardiorespiratory fitness and BMI were each strong (statistically significant) predictors. However, when all significant CVD risk factors were considered together at the same time, BMI was the only consistent and statistically significant predictor of LV mass index values for across all ECHO and CMR measurements and indices. Specifically, we found that a 1-unit increase in BMI was associated with 1 unit (g/m1.7) increase in the most commonly used LV mass index (g/ height in meters1.7) even after also considering age, hypertension, obstructive sleep apnea risk and cardiorespiratory fitness (table 3).

Table 3. Multivariate Statistical Models for assessing the effect of BMI on LV mass.

Variable	Model (by ECHO) Effect	Model (by CMR) Effect	Statistical Significance
Age, years	0.04	0.02	
Hypertension	1.06	1.29	
High Risk of OSA	0.76	0.15	***
Body Mass Index, Kg/m2	1.01	0.83	
Low CRF	-0.23	-0.96	

Conclusions & Discussion

This study of active U.S. career firefighters using ECHO and CMR measurements found BMI to be the strongest and most consistent independent predictor of LV mass index values. Therefore, our findings, in line with previous studies of the general population[1,2], support BMI as a major determinant of LV mass.

Given the epidemic level of obesity in the US fire service; it is very concerning that we found BMI to be the strongest predictor of LV mass in this population. Because obesity is associated with and often causes an individual to have multiple risk factors for heart disease[3,4], it probably explains why other factors like blood pressure and obstructive sleep apnea risk were weaker predictors because of their association with LV mass may be closely linked to obesity itself.[5] Considering our previous findings that obesity-associated SCD among younger firefighters was largely driven by an increased cardiac mass in SCD victims,[6] our results reinforce that decreasing obesity in the fire service will lower the risk of LV hypertrophy and therefore, of on-duty CVD events, particularly SCD. In agreement with findings that even small reductions on BMI may produce significant beneficial effects on metabolic syndrome and other CVD risk factors,[7,8] our results suggest that a 1-unit decrease in BMI, will reduce LV mass index by 1 unit (g/m1.7).

Our findings indicate that BMI is a major driver of LV mass, heart weight and LV wall thickness. Also, LV mass accounts for a greater proportion of total heart weight in diseased hearts compared to non-cardiac cases. Because obesity plays a central role in multiple risk factors, including hypertension, diabetes, high cholesterol it should be aggressively managed in the fire service. Additionally, our data indicates it is the most important factor in predicting cardiac enlargement. Therefore, we suggest targeted noninvasive screening for LV hypertrophy for obese firefighters to prevent on-duty CVD events in the fire service.

In conclusion, after normalizing ECHO- and CMR-measured LV mass for height, BMI was the strongest independent determinant of LV mass among male career firefighters. Previous research in the fire service has found that SCD among younger firefighters was largely driven by an increased cardiac mass in SCD victims as compared to controls, with 2/3 of SCD victims to be obese. Taken together with previous research our current findings suggest that reducing obesity will decrease the risk of LV hypertrophy and therefore, reduce on-duty CVD and SCD events in the fire service. Our findings support using cardiac echo, a noninvasive, reasonably priced and commonly available technique, for screening obese firefighters for the presence of LV hypertrophy as part of fire department medical surveillance.

References

1. Soteriades ES, Targino MC, Talias MA, Hauser R, Kawachi I, Christiani DC, Kales SN. Obesity and risk of LVH and ECG abnormalities in US firefighters. *J Occup Environ Med.* 2011;53:867-871.

2. Soteriades ES, Smith DL, Tsismenakis AJ, Baur DM, Kales SN. Cardiovascular disease in US firefighters: a systematic review. *Cardiol Rev.* 2011;19:202-215.

3. Soteriades ES, Hauser R, Kawachi I, Liarokapis D, Christiani DC, Kales SN. Obesity and cardiovascular disease risk factors in firefighters: a prospective cohort study. *Obes Res.* 2005;13:1756-1763.

4. Tsismenakis AJ, Christophi CA, Burress JW, Kinney AM, Kim M, Kales SN. The obesity epidemic and future emergency responders. *Obesity.* (Silver Spring) 2009;17:1648-1650.

5. Kales SN, Tsismenakis AJ, Zhang C, Soteriades ES. Blood pressure in firefighters, police officers, and other emergency responders. *Am J Hypertens.* 2009;22:11-20.

6. Yang J, Teehan D, Farioli A, Baur DM, Smith D, Kales SN. Sudden cardiac death among firefighters </=45 years of age in the United States. *Am J Cardiol.* 2013;112:1962-1967.

7. Mileski KS, Leitao JL, Lofrano-Porto A, Grossi Porto LG. Health-related physical fitness in middle-aged men with and without metabolic syndrome. *J Sports Med Phys Fitness.* 2015;55:223-230. 16. Elmer PJ, Obarzanek E, Vollmer WM, Simons-Morton D, Stevens VJ, Young DR, Lin PH,

8. Champagne C, Harsha DW, Svetkey LP, Ard J, Brantley PJ, Proschan MA, Erlinger TP, Appel LJ. Effects of comprehensive lifestyle modification on diet, weight, physical fitness, and blood pressure control: 18-month results of a randomized trial. *Ann Intern Med.* 2006;144:485-495.

Chapter 5

Summary of Findings and Recommendations to Reduce Cardiac Enlargement in the Fire Service

In the second group of data, LV hypertrophy and cardiomegaly estimates were based on the numerical values The goals of this work were:

1. to evaluate cardiac enlargement (including LV hypertrophy) and assess how the different non-invasive screening as well as forensic methods and reference ranges can affect distinctions between disease states and normality;
2. to provide more definitive prevalence estimates of cardiac enlargement among US firefighters; and
3. to identify the most significant clinical predictors of LV mass in this special occupational cohort.

Our findings provide important insights on the most appropriate method of assessing cardiac enlargement among the US firefighters. **The most important finding of our study is that BMI is an independent predictor and a major driver of LV mass, heart weight and LV wall thickness. Thus, significant reductions in on-duty CVD events could be realized by reducing obesity in the US fire service.**

Let's together lead the way forward to improve health & employment outcomes among US Firefighters.

Our understanding of CVD in the fire service has greatly increased over the past 15 years, with an increasing recognition in the role of cardiac enlargement. Although additional research is required to address remaining questions, this should not slow efforts to act on what we currently know. It is critical that we take aggressive steps to prevent and manage CVD to reduce cardiac-related deaths and disability in the fire service. To make significant progress, participation and buy-in at all levels is essential. Therefore, we have presented recommendations for reducing the risk of CVD, and specifically addressing obesity, that are targeted at different groups in the fire service as well recommendations for future research in the field.

Firefighters

Firefighters are ultimately the ones who must make the changes to reduce CVD in the fire service. Making these changes will require taking personal responsibility for one's health as well as adherence to policy and procedures. Firefighters must take an active role in reducing their risk for CVD. Based on current understanding of research, firefighters should:

1. Maintain a high level of physical fitness
2. Obtain an annual physical, even if it is not provided by your department
3. Routinely monitor blood pressure and control hypertension if present
4. Maintain/take steps to reach a healthy weight
5. Avoid tobacco use
6. Eat a healthy diet – consider the Mediterranean Diet as one proven to decrease CVD and cancer risk

Weight loss can improve OSA, blood pressure control and can reverse obesity related cardiac enlargement (including hypertrophy).

7. Avoid excessive use of alcohol
8. Get adequate sleep
9. In the presence of Obstructive Sleep Apnea, continuous positive airway pressure (CPAP) can produce reductions in LV hypertrophy.
10. In the presence of hypertension, anti-hypertensive drugs and particularly, angiotensin converting enzyme (ACE) inhibitors can produce echocardiographically-confirmed regression of LV hypertrophy.

Fire Department – Company Officer/Crew Boss

Company officers/crew bosses have a position of great influence and should act as intermediaries to reinforce existing policies and facilitate policy change when needed. Company officers/crew bosses should talk with their crews about specific actions firefighters can take to reduce their risk of CVD and should serve as a role model for firefighters. Based on current understanding of research, company offers/crew bosses should:

1. Encourage high levels of fitness
2. Promote good nutrition
3. Reinforce the importance of knowing your CVD risk factor profile and working to improve it
4. Promote a tobacco-free lifestyle
5. Encourage a supportive environment for meeting health and fitness goals

Fire Service Leadership – National Organizations

National organizations play a key role in promoting health and wellness in the fire service. These organizations influence legislation and policy decisions and set the national priorities for the fire service. Given previous findings that obesity-associated SCD among firefighters was largely driven by an increased cardiac mass in SCD victims compared to controls, our results show that decreasing obesity in the fire service will improve firefighters' cardiovascular risk profiles, including their risk of LV hypertrophy and significantly reduce on-duty CVD events, particularly SCD. Moreover, our data shows that BMI is a major driver of LV mass, heart weight and LV wall thickness. Our data also indicates that LV mass accounts for a greater proportion of total heart weight in diseased hearts compared to controls. Taken collectively our work indicates that obese firefighters are at increased risk for enlarged hearts and at greater risk for sudden cardiac events. This suggests that targeted noninvasive screening for LV hypertrophy is appropriate for obese firefighters.

Based on current understanding of research, it is recommended that fire service leaders take the following steps to prevent and manage CVD in the fire service:

1. Require pre-placement medical evaluations
2. Require annual medical evaluations
3. Require return to work evaluations
4. Implement physical fitness programs
5. Implement comprehensive wellness programs
6. Implement targeted screening for LV hypertrophy and cardiomegaly for obese firefighters, as well as those with uncontrolled or chronic hypertension or obstructive sleep apnea

Decrease obesity in the U.S. Fire Service

↓

Decrease risk of cardiac enlargement

↓

Reduce on-duty CVD and SCD events in the U.S. Fire Service

Strategies to Encourage Adoption of Recommendations

The recommendations presented above are both practical and attainable, albeit not without challenges. To effect change, recommendations must be adopted, and there are always obstacles that must be overcome in the process.

Strategies to ensure that firefighters receive education/counseling about medical conditions following a medical evaluation. That is, what can be done to ensure that firefighters are not simply being cleared for duty (i.e., how can a medical evaluation be kept from simply being a "cleared for duty" checklist that indicates everything is ok?)

- *Individual counseling after evaluation.*
- *Personal accountability.* Designate a member of the department to whom firefighters must report to ensure that firefighters are implementing the suggestions of the physician or doing the follow-up required.
- *Post-visit online education components.*
- *"Check up from the neck up" discussions.*
- *Group education.* (fellow firefighter with condition – what would you do?)

Importance of Lifestyle Choice to Reduce Risk of CVD (and Cancer)

- *Exercise/Physical fitness*
- *Healthy diet/Nutrition*
- *Tobacco cessation*
- *Limited smoke exposure*

Resources to help adopt/implement recommendations

1. IAFF/IAFC WFI Resource: http://bit.ly/1KSBwy0
2. U.S. Fire Administration Health and Wellness Guide for the Volunteer Fire and Emergency Services: http://bit.ly/2rvu11l
3. NVFC Heart-Healthy Firefighter Program: http://bit.ly/2seR8dG
4. The 16 Firefighter Life Safety Initiatives: http://bit.ly/2stcnL5
5. American Heart Association web resources: http://bit.ly/IO8ENf
6. NFPA Standards: 1500, 1582, 1583, and 1584

Suggestions/ Recommendations for Future Research

We believe that future studies are needed to validate the assessment of cardiac enlargement (including LV hypertrophy), and to identify the reference values that would be most appropriate for US firefighters considering the special CVD risk profiles of this unique occupational cohort. Moreover, future forensic studies are needed to directly compare total cardiac mass to left ventricular mass, in order to establish the relationship between the two. In this regard, national fire service organizations should advocate for LV mass to be measured at firefighter autopsies (cardiac and non-cardiac) to empower us to find more precise screening definitions for high risk based on LV mass. Finally, we suggest that future prospective studies of CVD events are needed to show that BMI is the most significant and useful prognostic indicator of CVD outcomes related to increased LV mass within the US fire service. We hope that this work will lead the way forward to improved health and employment outcomes among firefighters in the US.

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